

Dissociative Symptoms and Psychotic Features in Bipolar Disorder: Impact on Clinical Course and Treatment Response

Luca Steardo (✉ steardo@unicz.it)

Università degli studi Magna Graecia di Catanzaro Dipartimento di Scienze della Salute

<https://orcid.org/0000-0002-7077-3506>

Elvira Anna Carbone

Magna Graecia University of Catanzaro: Università degli Studi Magna Graecia di Catanzaro

Enrica Ventura

University of Magna Graecia: Università degli Studi Magna Graecia di Catanzaro

Renato de Filippis

University of Magna Graecia: Università degli Studi Magna Graecia di Catanzaro

Mario Luciano

University of Campania Luigi Vanvitelli: Università degli Studi della Campania Luigi Vanvitelli

Pasquale De Fazio

University of Magna Graecia: Università degli Studi Magna Graecia di Catanzaro

Research

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Abstract

Background

Dissociative symptoms are widely expressed in patients with bipolar disorder (BD) and may precede the onset of the disorder and be a marker of poor treatment response. In the present study we aimed: 1) to assess the relationship between dissociative symptoms and the onset of psychotic symptoms in patients with BD; 2) to assess clinical and socio-demographic characteristics more frequently associated with dissociative symptoms and the response to treatment with mood stabilizers.

Methods

One-hundred patients diagnosed with BD were enrolled in this study. They underwent a semi-structured interview to collect socio-demographic and clinical characteristics. Dissociative Experiences Scale-II (DES-II) and ALDA scale were used to assess dissociative psychopathologies and response to treatment with mood stabilizers respectively.

Results

Forty-four percent of patients reported psychotic symptoms on the DES-II scale; BD I patients had a higher total DES-II score than BD II patients. Dissociative symptoms presented a direct correlation with the total number of episodes ($p < .000$), antidepressant switch to mania ($p < .000$), seasonality ($p < .000$), aggression ($p < .000$), and mixed states ($p < .000$). Higher DES-II scores were reported by patients with poor response to treatment.

Conclusions

Dissociative phenomena are closely related to the presence of psychotic symptoms in BD, especially in BD I. In a future perspective, this association could represent a diagnostic indicator of BD I have given the close association with psychotic symptoms. Our study shows that several clinical variables transversely indicate a poor response to treatment with mood stabilizers, a worse course of illness, and the presence of dissociative symptoms.

Introduction

Dissociative phenomena include a variety of processes and phenomena along a continuum from adaptive coping strategies to more pathological states (Holmes et al. 2005). The Diagnostic and Statistical Manual of Mental Disorders 5th edition (DSM-5) defines dissociative symptoms as “a disruption of and/or discontinuity in the normal integration of consciousness, memory, identity, emotion, perception, body representation, motor control, and behavior” and identifies five components of

dissociation: depersonalization, derealization, amnesia, identity confusion and identity alteration (American Psychiatric Association 2013). Two major theories have been proposed to explain the etiology of dissociative symptoms. The *“trauma theory”* considers dissociation as the coping strategy adopted to deal with severe anxiety symptoms associated with traumatic experiences (Lee et al. 2012; Şar 2017; Stein et al. 2013). The *“disrupted sleep theory”* considers the distortion of cognitions, emotions, and sensations associated with prolonged sleep deprivation as the trigger for the experience of dissociative symptoms (Van Heugten-Van Der Kloet et al. 2015; van der Kloet et al. 2012).

It has been reported that dissociative symptoms are widely expressed in patients with bipolar disorder (BD), in particular in those reporting the presence of significant trauma in childhood (Aas et al. 2016). Moreover, disruption in circadian rhythms, usually reported by patients with BD, could be implicated in the manifestations of dissociative symptoms due to severe and persistent insomnia, that alters the physiologic process of memorization (Khan et al. 2018). Therefore, both trauma exposure and sleep fragmentation can lead to cognitive dysfunctions affecting a patient's coping skills and increasing the occurrence of dissociative symptoms (Cipriani et al. 2017; Thompson et al. 2015).

Current evidence suggests that the assessment of dissociative symptoms could be useful in differentiating patients with BD from those with unipolar major depression during depressive episodes. It has been reported that patients with BD are more likely to report dissociative symptoms than those patients with unipolar depression (Chatterjee et al. 2018). Moreover, dissociative symptoms may precede the onset of the disorder and could be a risk factor for the development of BD (Hariri et al. 2015). Besides, dissociative symptoms are frequently associated with a worse prognosis and a greater number of mood fluctuations (Aas et al. 2016; Amare et al. 2020; Depp et al. 2016; Mula et al. 2009; Yayla et al. 2015). Moreover, available data suggest that the presence of dissociative symptoms is considered a marker of poor treatment response in BD (Dualibe and Osório 2017). Despite dissociative symptoms can have a potential impact on the psychopathological burden of patients with BD, only a few studies have assessed the relationship between dissociative and psychotic symptoms and treatment response to mood stabilizers.

The aims of the present study are twofold: 1) to assess the relationship between the presence of dissociative symptoms and the onset of psychotic symptoms in patients with BD; 2) to assess those clinical and socio-demographic characteristics more frequently associated with dissociative symptoms and to assess the potential role of dissociative symptoms on response to treatment with mood stabilizers.

Methods

Participants and procedures

This is a naturalistic observational study. Patients were consecutively recruited at the psychiatric outpatients unit of the University of Catanzaro, from May 2019 to January 2020. Patients were included in the study if they met the following criteria: (1) age between 18 and 65 years, (2) diagnosis of type-I or

type-II bipolar disorder according to the Diagnostic and Statistical Manual of Mental Disorders-fifth edition (DSM-5) (First et al. 2016). No other inclusion criteria were selected to obtain a sample as similar as possible to patients routinely seen in the real world. The following exclusion criteria were applied: 3) diagnosis of dementia, intellectual disability, epilepsy, or another medical condition associated with psychiatric symptoms; 3) difficulty in understanding the questions asked; 4) alcohol and substance abuse or dependence.

After receiving a full description of the study aims, all participants provided written informed consent according to the Ethical Committee's guidelines. The study was carried out in accordance with the latest version of the Declaration of Helsinki and was approved by the local Research Ethics Committee of the University of Catanzaro "Magna Græcia" (N. 307).

Assessments

Socio-demographic and clinical characteristics

Recruited patients underwent a semi-structured interview to collect socio-demographic and clinical characteristics using an ad hoc schedule. Data on age, gender, civil status, education, occupation, family history of psychiatric illnesses, medical or psychiatric comorbidity, onset and longitudinal course of the disorder (number of depressive/hypo/manic episodes), suicidal ideation, and previous psychiatric hospitalizations and ongoing treatment were recorded.

Dissociative Experiences Scale-II (DES-II)

DES-II is a self-assessment measure developed by Bernstein and Putnam (Bernstein and Putnam 1986) and translated into Italian for the screening of dissociative psychopathologies. It consists of 28 items that describe dissociative experiences (amnesia, absorption, depersonalization, and derealisation). Patients are asked to indicate with a percentage the frequency they have experienced them (0% never; 100% always). The final score is given by the sum of the scores of the individual items divided by the number of total items and can therefore be included between 0 and 100: scores greater than 30 are associated with a diagnosis of dissociative disorder.

ALDA scale

The ALDA rating scale assesses response to treatment with mood stabilizers in bipolar patients (Scott et al. 2019; Scott et al. 2017). The scale comprises two sections to rate lithium response Section A Section B, and a total score. Section A evaluates the effectiveness of the ongoing treatment with a mood stabilizer, with a score ranging from 1 to 10 (1= no response; 10= excellent response); Section B consists of 5 items to be scored from 0 to 2 to be subtracted from criterion A. The five subdomains of criterion B consider the number of episodes before the start of treatment, the frequency of episodes outside the treatment period, the duration of treatment, compliance with therapy, and the presence of polypharmacy. The total score on the Alda scale is divided into three sub-items: 0-3 = poor response; 4-6 = moderate response; 7-10 =good response

Statistical analyses

Data were analysed using the Statistical Package for the Social Sciences, version 26.0 (SPSS Inc., Chicago Illinois) and are presented as averages, standard deviations (SD), frequencies, and percentages (%), as appropriate. The Kolmogorov-Smirnoff test was used to assess the normality of the distribution of our sample. Given the not normal distribution, Pearson's correlation and U-Mann Whitney were used to testing the correlation between dissociation and clinical variable. Tukey's test was used to verify the correlation between the Alda scale score and dissociative symptoms. Linear regression analyses using DES-II total score as the dependent variable was performed. Independent variables were selected among those with a positive association at the univariate analyses. The level of statistical significance was set at $p < 0.05$.

Results

The total sample consisted of 100 patients. Fifty percent of the sample was male, aged 46.5 ± 13.94 . Fifty-five percent of the sample had a diagnosis of BD I (Table 1). The majority of patients are married (48%), employed (60%), and with a high level of education (77%). Patients reported high familiarity rates for psychiatric disorders (68%) and medical comorbidities (60%) (more frequently endocrinological and cardiological ones). The onset of BD was at 27.30 ± 9.85 years with a duration of illness of 19.04 ± 12.99 years. Almost all patients reported at least a depressive episode (mean depressive episodes lifetime 5.44 ± 5.02); about half of the sample at least on a manic episode (mean manic episodes lifetime 3.84 ± 2.87) and 94% of patients experienced hypomanic episodes (mean hypomanic episodes lifetime 3.19 ± 3.00). One-third of patients reported suicidal ideation/suicidal attempts (mean number of suicide attempts 1.03 ± 0.72) (Table 1).

Table 1
Socio-demographic and clinical characteristic of total sample

	Sample (N = 100)	
Socio-demographic characteristics	Age, M (\pm DS)	46.50 (13.94)
	Gender, male, N (%)	50 (50)
	Years of education M (\pm DS)	13.3 (\pm 3,5)
	Having partner, yes, N (%)	48 (48)
	Employed, yes, N (%)	60 (60)
	Diagnosis of BD-I, N (%)	55 (55)
	Family history of psychiatric disorder, yes N (%)	68 (68)
Clinical variables	Age of onset M (\pm DS)	27.3 (\pm 9.85)
	Age first psychiatric contact M (\pm DS)	29.97 (\pm 10.06)
	Age first depressive episode M (\pm DS)	27.67 (\pm 9.95)
	Age first manic episode M (\pm DS)	28.13 (\pm 7.09)
	Age first hypomanic episode M (\pm DS)	30,2 (\pm 8,7)
	Age first mixed episode M (\pm DS)	31.57(\pm 10.01)
	Tot number of depressive episodes M (\pm DS)	5.44 (\pm 5.02)
	Tot number of manic episodes M (\pm DS)	3.84 (\pm 2.87)
	Tot number of hypomanic episodes M (\pm DS)	3.19 (\pm 3)
	Tot number of episodes M (\pm DS)	10.5 (\pm 9.75)
	Tot number of episodes during last year M (\pm DS)	0.77 (\pm 0.76)
	Suicide attempts, yes, N (%)	30 (30)
	Number of suicide attempts, M (\pm DS)	1.03 (\pm 0.72)
	Aggressive behaviors, yes, N (%)	57 (57)
	Psychotic symptoms, yes, N (%)	55 (100)
	Seasonality, yes, N (%)	48.4 (100)
	Tot number of hospitalizations, M (\pm DS)	0,7 (\pm 0,9)

Sample (N = 100)		
	Illness duration M (\pm DS)	19.04 (\pm 12.99)
	Course of illness, regular, N (%)	32.3 (100)
	Anxious Features, N (%)	66.3 (100)
	Mixed features, N (%)	50.6 (100)
	Antidepressant switch, yes, N (%)	29 (29)
ALDA Total score	Poor response	40 (100)
	Moderate response	48 (100)
	Good response	12 (100)
DES-II	Psychotic symptoms, yes M (\pm DS)	51.82 (\pm 2.2)
	Psychotic symptoms, no M (\pm DS)	14.31 (\pm 1.9)
BD I: type I bipolar disorder; BD II: type II bipolar disorder; DES-II: Dissociative Experience Scale-II.		

About half of patients had a seasonal trend (46%), aggressive behaviors (57%), anxiety (59%), or mixed characteristics (45%). Manic/hypomanic switches due to antidepressant treatment were observed in 29% of patients. 23% of patients experienced substance abuse over a lifetime.

Forty-four percent of patients reported psychotic symptoms on the DES-II scale (30%). BD I patients had a higher total DES-II score than BD II patients (30.82 ± 11.3 vs 18.04 ± 5.6). Patients with BD I with psychotic symptoms ($n = 44$) had a mean DES-II score of 51.1 ± 11.3 , compared to patients with BD I without psychotic symptoms ($n = 45$) have an average DES-II score of 18.0 ± 15.6 ($p < .001$). A higher DES-II score in BD I patients with psychotic symptoms compared to the other subgroup (BD without psychotic symptoms) ($p < .001$) has been reported (Table 2).

Table 2
Correlation analysis Dissociation and Psychotic symptoms in BD

	F	Df	Sig.	η^2
Correct model	86,700	2	,000	,641
Intercept	476,001	1	,000	,831
Diagnosis	2,860	1	,094	,029
Psychotic symptoms	83,911	1	,000	,464
Diagnosis * psychotic symptoms		0		0,000

At correlation analyses, dissociative symptoms presented a direct correlation with the total number of episodes ($p < .000$), antidepressant switch to mania ($p < .000$), seasonality ($p < .000$), aggression ($p < .000$), and mixed states ($p < .000$) (Table 3–4). Logistic regression analyses reported that the presence of psychotic and mixed features can be considered predictors of dissociative symptoms ($p < .000$) (Table 5). Tukey post-hoc test revealed that higher DES-II scores were reported by patients with poor response to treatment, while milder dissociative symptoms were observed in patients with an excellent therapeutic response ($p < .000$) (Table 6).

Table 3
U-Mann Whitney correlation of clinical variables and DES-II total score

Variables	DES-II
Diagnosis	0.000
Psychotic symptoms	0.000
Suicide	0.000
Antidepressant switch	0.000
Seasonality	0.000
Mixed characteristics	0.000
Anxious characteristics	0.000
Aggressive behavior	0.000
DES II: Dissociative Experience Scale-II.	

Table 4
Person's correlation of clinical variables and DES-II total score

	DES Total Score
2. Tot number of episodes	,533**
3. Tot number of hypomanic episodes	,313**
4. Tot number of manic episodes	,494**
5. Tot number of depressive episodes	,532**
6. Age at onset	-0,063
** $p < .01$; DES-II: Dissociative Experience Scale-II.	

Table 5
Linear regression model

Dependent variable	Independent variable	B	Standard error	Beta	t	p	
DES-II	Psychotic features	18,027	4,490	,494	4,014	,000*	
	Mixed features	10,074	4,662	,259	2,161	,038*	
	Family History	4,329	4,142	,109	1,045	,303	
	Age of first contact	,223	,415	,079	,538	,594	
	Age at onset	-,385	,468	-,120	-,824	,416	
	Clinical course	-1,930	1,494	-,127	-1,292	,205	
	Number of depressive episodes	,807	1,431	,274	,564	,576	
	Number of manic episodes	-,703	1,593	-,097	-,441	,662	
	Number of hypomanic episodes	-,503	1,511	-,112	-,333	,741	
	Mania induced by antidepressant	-1,211	3,670	-,034	-,330	,743	
	Suicide	7,925	4,154	,224	1,908	,065	
	Aggressive behavior	-4,141	4,207	-,095	-,984	,332	
	Anxious features	3,254	5,151	,072	,632	,532	
	DES-II: Dissociative Experience Scale-II.						

Table 6
Tukey test

Alda scale total score	DES-II total score M (± DS)	p
Poor	44,64 (18,65)	0,000
Moderate	23,95 (19,3)	0,000
Good	12,02 (18,18)	0,000
*. p < 0.05; dependent variable: DES-II Total score.		
DES-II: Dissociative Experience Scale-II.		

Discussion

The main finding of our study is the presence of a stable correlation between dissociative symptoms and psychotic features in BD. Moreover, such correlation is related to clinical severity as shown by the higher DES-II total score in patients with a higher number of episodes, aggressive behaviors, seasonality, mixed features, and poor response to mood stabilizers.

Our study is the first to demonstrate that the occurrence of dissociative dimension is higher in BD I, especially in those with psychotic features and in those who present a greater clinical severity (Latalova et al. 2011; Montant et al. 2014; Rafiq et al. 2018).

In our sample, 55% of patients developed psychotic symptoms, and among this group, there were higher levels of dissociative symptoms, combined with a greater psychopathological load and lack response to mood stabilizers (Belteccki et al. 2018). These results could be explained by the fact that dissociative symptoms are more expressed in patients with psychotic symptoms as demonstrated for other mental disorders (Schäfer et al. 2012). According to Allen et al (Allen et al. 1997), who developed the theory of “dissociative detachment”, dissociative phenomena “undermines the individual's grounding in the outer world”, rendering the individual susceptible to developing psychotic features. Moreover, other authors have highlighted the inverse relationship in which dissociation is a defense against the disorganization and acute distress generated by psychosis (Giese et al. 1997). Other possible mechanisms might be the early trauma exposure that predisposes to a higher psychopathological load among different psychiatric disorders, including BD (Carbone et al. 2019; Wang et al. 2021). However, we did not assess the impact of trauma in this study and therefore this explanation remains speculative. Moreover, several clinical variables emerged as strongly associated with the presence of dissociative symptoms. The higher number of lifetime episodes, independently from the episode polarity, is associated with a higher total score. It may be that with the increasing of illness episodes patients’ skills to achieve a functional recovery during the euthymic phases become compromised and, as in advancing age, it correlates with a decrease in cognitive abilities. As to the latter, several studies reported that cognitive dysfunction is associated with a higher number of relapses, a higher number of hospitalizations, dissociative symptomatology, and the worst functional outcome (López-Villarreal et al. 2020). This could partially explain our findings and the association between dissociation and the high number of episodes, but the data available in the literature are still scarce and a more dept analysis of the argument is needed.

Moreover, mixed characteristics are associate with a higher DES-II total score. Mixed features are associated with a lack of response to mood stabilizers in BD and this could explain why patients with dissociative are refractory to treatment. (Swann 2017). Furthermore, mixed features are often triggered by antidepressant therapy, and this feature is also associated with greater dissociative symptomatology as demonstrated by the correlation analysis. Seasonality, in our sample, is associated with dissociative symptoms. This is the first study demonstrating such association. This finding could be explained in the light that a seasonal pattern is associated with a higher number of relapses therefore to worse prognosis (Aguglia et al. 2020; Brandl et al. 2018). Moreover, in our sample, aggressive behaviors are associated with the development of dissociative symptomatology. These behaviors are often related to high levels of impulsivity (Strakowski et al. 2010) and cognitive dysfunction that could explain the higher DES-II scores

in patients. The analysis of variance shows that poor response to treatment with mood stabilizers correlates with high DES-II scores. This issue is explainable for two reasons. Patients with worse responses to treatment will experience a worse outcome, a lack of functional and cognitive recovery, and the onset of dissociative symptoms. Secondly, the clinical variables associated with dissociative symptomatology are superimposable with those that predispose to refractoriness to drug treatment.

However, the study also has some important limitations, one being the small sample size. Moreover, the cross-sectional design of the study limits conclusions about reverse causality. A longitudinal evaluation of dissociative symptoms will allow us to clarify the association between dissociative symptoms and clinical variables. However, we have planned follow-up assessments to counterbalance this limitation. Another limitation is represented by the recall bias of incompleteness and imprecision of the patients' memories and, ultimately, the phases of disorder; in fact, not all patients were in the worst phase during the interview. Therefore, we planned a further study in which we will include only patients in the acute phase of the illness.

Conclusions

Dissociative phenomena are closely related to the presence of psychotic symptoms in BD, especially in BD I. In a future perspective, this association could represent a diagnostic indicator of BD I have given the close association with psychotic symptoms. Our study shows that several clinical variables transversely indicate a poor response to treatment with mood stabilizers, a worse course of illness, and the presence of dissociative symptoms. Therefore, we consider it extremely important to evaluate the presence of ongoing dissociation in BD to direct the clinician to plan the most appropriate treatment. Future studies should investigate in greater depth the causes underlying this association and the most appropriate therapeutic strategy to reduce the impact that these symptoms have on the course of BD.

List Of Abbreviations

BD: Bipolar Disorder; DSM-5: DES-II: Dissociative Experiences Scale-II; Diagnostic and Statistical Manual of Mental Disorders 5th edition.

Declarations

Ethics approval and consent to participate

All participants provided written informed consent according to the Ethical Committee's guidelines. The study was carried out in accordance with the latest version of the Declaration of Helsinki and was approved by the local Research Ethics Committee of the University of Catanzaro "Magna Græcia" (N. 307).

Consent for publication

N/A

Availability of data and material

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Conceptualization, LS; methodology, LS and ML; formal analysis, LS and ML.; investigation, LS, EAC, RDF; data curation, EV and RDF; writing the original draft preparation, LS, EAC, ML; writing and review and editing, ML, PDF. All authors read and approved the final manuscript.

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